Remarks

Claims 1-55 are pending. Claims 56-94 have been added. Claims 1-55 have been canceled.

Regarding the Amendments

Upon entry of the above amendment, claims 56-94 will be pending. Claims 1-55 have been cancelled without prejudice or disclaimer. Applicants reserve the right to prosecute the subject matter of the cancelled claims in a continuation, continuation-in-part or divisional application.

New claims 56-94 have been added to more clearly define the scope of protection being sought. Applicants assert that no new matter has been added. New claims 56-94 are directed to methods of using the mammalian tissue model for screening for an anti-tumour substance. Support for new claims 56-94 can be found throughout the specification as filed, for example, in the claims as originally filed.

Response to Restriction Requirement

Claims 1-55, currently pending in this application, stand restricted under 35 U.S.C. 121 and 372, into Groups I, II, III and IV, as defined in the Office Action. Applicants elect, with traverse, Group II, relating to methods of using the claimed model for screening for an anti-tumour substance. Applicants assert that new claims 56-94, submitted herewith, are also drawn to methods of screening for an anti-tumour substance using the mammalian tissue model and, therefore, should be examined with elected Group II.

Remarks

The Examiner has alleged that the instant application contains the following groups of

inventions that are not so linked as to form a single inventive concept under PCT Rule 13.1:

I. Claims 1-42, drawn to a mammalian tissue model comprising cells of at least two different phenotypes wherein the cells of at least one phenotype form 3D aggregates.

II. Claims 43-48, drawn to a first method of using the claimed model for screening for an anti-tumour substance.

III. Claims 49-51, drawn to a second method of using the claimed model for screening a substance modulating gap junction intercellular communication.

IV. Claims 52-55, drawn to a third method of using mammalian tissue simulation model for predicting biological characteristics.

The Examiner alleged that the above Groups do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, Groups I-IV lack the same or corresponding special technical features. The Examiner also alleged that the instant application contains claims drawn to more than one permissible combination of categories of inventions, and further alleged that the "special technical feature" that defines the contribution which each of the claimed inventions, considered as a whole, makes over the prior art, is known in the prior art. Specifically, the Examiner has cited U.S. Patent No. 5,518,915, and alleged that this patent discloses a 3D mammalian tissue model comprising cells of different phenotypes.

Applicants respectfully traverse the above restriction for the following reasons. Applicants assert that the single general inventive concept unifying the currently pending claims is a mammalian tissue model, and that the instantly claimed subject matter considered as a whole, shares the same technical features, as required by PCT Rule 13.2, in that the mammalian tissue model comprises mammalian cells of at least two different phenotypes in predetermined

initial proportions and 3-dimensional aggregates formed from cells of at least one phenotype, which allows for assessment of various biological characteristics, such as cell proliferation kinetics or gap junction intercellular communication (see, for example, page 12, lines 12-28, of the application as filed). The mammalian tissue model can be formed in the absence or presence of a solid support (see, for example, page 6, lines 16-27, of the specification as filed) and can comprise various combinations of cells including tumour cells, epithelial cells, endothelial cells and stromal cells (see, for example, page 7, lines 2-8, of the specification and the claims as originally filed). Applicants assert that, contrary to the Examiner's allegation, these special technical features were not known in the art at the time the instant application was filed. For example, U.S. Patent No. 5,518,915, cited by the Examiner, discloses only a very specialised type of *in vivo* tissue model that comprises, *as an essential element*, a matrix of stromal cells that *must be pre-established on a 3-dimensional solid support*. As such, other cell types can only be grown on this supported stromal matrix once it has been established. U.S. Patent No. 5,518,915 does not disclose a mammalian tissue model comprising cells of at least two different phenotypes in predetermined initial proportions, in which the cells of at least one phenotype form 3-dimensional aggregates, nor does U.S. Patent No. 5,518,915 disclose any tissue models that can be formed in the absence of a solid support or without the requirement for pre-establishing a stromal matrix.

Furthermore, as pointed out by the Examiner, it is permissible for an application to include claims directed to combinations of categories (for example, to a product and a process of use). In this regard, the Examiner is also directed to Section (e)(i) of Annex B of the PCT Administrative Instructions, which permits, for the purposes of determining unity of invention

under Rule 13.2 "claims of different categories in the same international application: (i) in addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of said product (emphasis added)."

Applicants accordingly assert that unity of invention does exist under the terms of PCT Administrative Instructions, Annex B, Section (e)(i), since the criteria for combinations of claims of different categories has been fulfilled, namely, Group I is directed to a given product, *i.e.* a mammalian tissue model, and Groups II-IV are directed to methods of using said product, *i.e.* methods of using this product to screen for substances that affect a biological characteristic, for example, anti-tumour or gap junction modulating substances (Groups II and III), and methods for predicting a biological characteristic based on a simulation model of mammalian tissue developed through the use of the product. In this regard, Applicants respectfully remind the Examiner that during International Preliminary Examination, the PCT Examiner considered that under PCT Rule 13.2, claims 1-55 were directed to two inventions only, *i.e.* claims 1-51 (Invention 1) and claims 52-55 (Invention 2).

Further, the guidelines set forth in MPEP § 803 clearly indicate that there are two criteria for a proper requirement for restriction between patentably distinct inventions: (A) the inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05 - § 806.05(i)); and (B) there must be a serious burden on the Examiner if restriction is required (see MPEP § 803.02, § 806.04(a) - § 806.04(i), § 808.01(a), and § 808.02). If the search and examination of an entire application can be made without serious burden, the

Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Applicants assert that the claims of Groups I-IV are connected by a single, searchable unifying relationship as discussed above and, as such, do not recite independent inventions or inventions that are distinct as claimed. In view of this single, searchable unifying relationship, Applicants assert that the Examiner would not be seriously burdened by searching and examining the claims of Groups I-IV in a single application. Moreover, Applicants note that claims 43-51 of Groups II and III, merely represent additional embodiments of the subject matter claimed in instant claims 1-42 (Group I), given the former claims refer to and encompass all of the features of claim 1.

In summary, Applicants assert that not only has the requirement of unity of invention as defined under PCT Rule 13.1 and 13.2 been met in that the claims of Groups I-IV belong to permissible combinations of different categories and share the same special technical features, as described above, but also that claims 1-55 are connected by a single, searchable unifying relationship (*i.e.* a mammalian tissue model) and that the Examiner would not, therefore, be seriously burdened by searching and examining the claims of these groups in a single application. Accordingly, Applicants respectfully request withdrawal of the restriction of claims 1-55.

Solely in order to expedite prosecution of the instant application, however, Applicants have withdrawn claims 1-55, currently on file, without prejudice or disclaimer, and submit herewith new claims 56-94, which relate to elected Group II.

Election of Species

Claims 1-42 (Group I), currently pending in this application, stand further restricted under PCT Rule 13.1 into three series of species, as defined in the Office Action. Although, as indicated above Applicants have elected, with traverse, Group II to which the additional species restriction does not apply, in order to comply with the Examiner's requisition in the Office Action, Applicants also elect, with traverse, the following species. From the cell series species: 3) cells of a first phenotype that are epithelial (claims 33-36); from the support series species: 2) tissue model in the absence of solid support (claim 3); and from the chemical compound series: 2) tissue model comprising phototoxic agent (claims 40-42). Applicants note that the Examiner indicated that group 2) of the chemical compound series species comprises claims 40-43. Claim 43, currently on file, however, is drawn to a method of screening for an anti-tumour substance. Applicants assume that the Examiner intended to recite claims 40-42 and have made the above election on this basis.

Remarks

The Examiner has further alleged that the instant application contains claims within Group I that are directed to more than one species as follows:

- cell series species: cells of a "first" phenotype that are 1) endothelial cells (claims 18-24); 2) stromal cells (claims 25-30); and 3) epithelial cells (claims 33-36).

- support series species: 1) tissue models comprising a solid support (claims 4 and 5); and 2) tissue models in the absence of a solid support (claim 3).

- chemical compound series species: 1) tissue models comprising mitomycin (claim 39);

and 2) tissue models comprising phototoxic agent (claims 40-43).

The Examiner alleged that the species do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features. The Examiner further alleged that the "special technical feature" that defines a contribution which each of the claimed inventions, considered as a whole, makes over the prior art, is known in the prior art. Specifically, the Examiner has cited U.S. Patent No. 5,518,915, and alleged that this patent discloses a 3D mammalian tissue model comprising a solid matrix support, various cells including epithelial cells and additional chemical compounds.

Applicants respectfully traverse the Examiner's restriction for the following reasons. Firstly, for the reasons outlined above with respect to claims 1-55, Applicants assert that claims 1-42 are unified by a single general inventive concept, *i.e.* a mammalian tissue model, and that the instantly claimed subject matter, considered as a whole, shares the same special technical features, as required by PCT Rule 13.2, in that the mammalian tissue model comprises mammalian cells of at least two different phenotypes in predetermined initial proportions and 3-dimensional aggregates formed from cells of at least one phenotype, which allows for assessment of various biological characteristics, such as assessment of cell proliferation kinetics or gap junction intercellular communication. As discussed above, these special technical features are not disclosed by U.S. Patent No. 5,518,915, which describes only a very specialised type of *in vivo* tissue model that comprises, *as an essential element*, a matrix of stromal cells pre-established on a 3-dimensional solid support and does not disclose a mammalian tissue model comprising cells of at least two different phenotypes in predetermined initial proportions, or any tissue models that can be formed in the absence of a solid support and without the requirement of pre-establishing a

stromal matrix. Accordingly, as the cited art does not disclose each and every element of the *in vitro* model of mammalian tissue as recited in independent claim 1, currently on file, it follows that the cited art cannot describe each and every element of dependent claims 3-5, 18-30, 33-36 and 39-42 and the Examiner's argument that the cited art describes a solid matrix support, various cells including epithelial cells and additional chemical compounds thus becomes moot. Applicants, however, respectfully direct the Examiner's attention to the fact that the additional compounds described at Col. 5, lines 44-47, of U.S. Patent No. 5,518,915 are growth supplements, which are added to, or used to coat, the solid support upon which the stromal matrix is established. U.S. Patent No. 5,518,915 does not describe any chemical agents that can be used to treat cells of one phenotype prior to forming a 3-dimensional aggregate as recited in instant claim 37, upon which claims 39-42 depend.

Moreover, as claims 1-42 all relate to a single general inventive concept, as described above, these claims are linked by a single, searchable unifying relationship and Applicants assert that that there would thus be no serious burden on the Examiner to search and examine all the claims of Group I, *i.e.* claims 1-42, together in a single application.

For the reasons set forth above, Applicants assert that the Examiner has failed to meet the criteria for proper restriction according to PCT Rule 13.1 and 13.2 and under the guidelines of MPEP and, therefore, respectfully requests that the Examiner withdraw the restriction of claims 1-42.

In the event that the above arguments are not persuasive, however, Applicants elect the following species in the above-noted series: epithelial cells, tissue model in the absence of a solid support and tissue model comprising a phototoxic agent.

Submitted herewith is an Information Disclosure Statement, an Information Disclosure Statement List, copies of cited non-patent publications, a corrected statement under 37 C.F.R. § 3.73(b), a request for a 5 month extension of time, and a Credit Card Payment Form PTO-2038 authorizing payment in the amount of $2,160.00, representing the fee for a large entity under 37 C.F.R. § 1.17(a)(5) for a 5 month extension of time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Robert A. Hodges — Date 10/25/2005